

## REMARKS

### Summary of Office Action

As an initial matter, Applicants note with appreciation that the Examiner has acknowledged the receipt of the recently filed priority documents.

Applicants further note that on Form PTO-1449 filed August 30, 2004 the previous Examiner has failed to initial Cite No. 14, i.e., DE 100 02 725. Accordingly, the present Examiner is respectfully requested to return another Form PTO-1449 which has Cite No. 14 initialed with the next communication from the Patent and Trademark Office.

The specification is again objected to.

Claims 1, 2 and 5-11 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Harding et al., U.S. Patent No. 5,705,144 (hereafter "HARDING") in view of Schonrock et al., U.S. Patent No. 6,296,857 (hereafter "SCHONROCK").

While not specifically stated in the present Office Action, it is assumed that as set forth in the previous Office Action, claims 1 and 2 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over several claims of copending Application Nos. 11/087,395, 11/547,104, 10/871,819 and 11/157,946.

### Response to Office Action

Reconsideration and withdrawal of the rejections of record are respectfully requested in view of the following remarks.

***Response to Objection to Specification***

The specification is again objected to because of the allegedly improper identification of trademarks therein.

The Examiner's corresponding comments in the present Office Action are noted. Applicants respectfully request to hold this objection in abeyance until the Examiner has indicated allowable subject matter.

***Response to Rejection of Claims under 35 U.S.C. § 103(a)***

Claims 1, 2 and 5-11 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over HARDING in view of SCHONROCK. The rejection essentially merely comments on Applicants' arguments in response to the previous Office Action. The previous Office Action alleged that HARDING teaches a composition for lightening skin which comprises a dioic acid of a general structure which encompasses 8-hexadecene-1,16-dicarboxylic acid and that HARDING further teaches that the composition further contains cosmetic adjuncts such as antioxidants. With respect to folic acid as an antioxidant, the previous rejection relied on SCHONROCK, asserting that this document teaches a method for cosmetically lightening large areas of the skin comprising the antioxidant folic acid. In view thereof, the previous Examiner essentially took the position that, absent a showing of unexpected results, it would allegedly have been obvious to one of ordinary skill in the art to incorporate folic acid into the compositions of HARDING. The previous rejection further asserted that the motivation to combine the compounds of HARDING with the compounds of SCHONROCK arises from the fact that the compositions of these two documents are both used for lightening large areas of the skin.

Applicants respectfully traverse this rejection again. Specifically, it is pointed out that according to, e.g., claim 1 of HARDING the dioic acids for use in combination with retinol or a derivative thereof are of general formula



wherein a is an integer of from 6 to 20 and b is an integer of from 8 to 40.

Even if only saturated dioic acids are considered this formula encompasses 15 different acids (with a total of 8 to 22 carbon atoms). The shortest mono-unsaturated acid ( $a = 6$ ) already has three isomers, each of which has two stereoisomers (cis- and trans- isomers). The longest mono-unsaturated acid ( $a = 20$ ) has 10 isomers, each with two stereoisomers. Accordingly, the above formula encompasses a total of  $3 + 4 + 4 + 5 + 5 + 6 + 6 + 7 + 7 + 8 + 8 + 9 + 9 + 10 + 10 = 101$  different mono-unsaturated acids (not counting stereoisomers), 8-hexadecene-1,16-dicarboxylic acid being only one example of the altogether 7 different hexadecene-1,16-dicarboxylic acid isomers. In the case of di-unsaturated dioic acids the number of possible isomers which are encompassed by the above formula is significantly higher than in the case of saturated and mono-unsaturated dioic acids. For example, for  $a = 6$ , there are already six isomeric di-unsaturated dioic acids (without stereoisomers). For  $a = 20$  there are 108 isomeric di-unsaturated dioic acids (without stereoisomers). Accordingly, the above formula apparently encompasses about thousand different saturated, mono-unsaturated and di-unsaturated dioic acids (without counting stereoisomers).

The rejection does not explain why one of ordinary skill in the art would have had an apparent reason to pick from the host of saturated, mono-unsaturated and di-unsaturated dioic acids which are encompassed by the general formula provided by HARDING one specific compound, i.e., 8-hexadecene-1,16-dicarboxylic acid, which is not only not mentioned in HARDING (in contrast to many other dioic acids) but whose method of preparation is not disclosed in HARDING, either. In

this regard, it is noted that according to HARDING, C<sub>8</sub>-C<sub>16</sub> saturated dioic acids are available commercially from chemical suppliers (col. 3, lines 28-29) and C<sub>17</sub>-C<sub>22</sub> saturated or unsaturated dioic acids can be manufactured by fermentation using certain yeasts (col. 3, lines 30-33).

With respect to C<sub>8</sub>-C<sub>16</sub> unsaturated dioic acids HARDING mentions in col. 3, lines 43-46 that these acids can be produced using the method disclosed in EP 341 796, further details of which are provided in the following passages of this document. According to col. 4, lines 1-26 of HARDING, it can be predicted that by using oleic acid as a substrate in this method, a mixture of 8 different mono-unsaturated dicarboxylic acids may be produced, whereas linoleic acid is expected to afford a mixture of 13 di-unsaturated dicarboxylic acids and linolenic acid is predicted to afford a mixture of 12 di- and tri-unsaturated dicarboxylic acids. None of these expected or predicted mixtures contains an isomer of 8-hexadecene-1,16-dicarboxylic acid. Moreover, even if one of these mixtures happened to contain 8-hexadecene-1,16-dicarboxylic acid, one of ordinary skill in the art would understand that it likely is difficult to separate the components of these complex mixtures of dioic acids from each other.

In view of the foregoing it is not surprising that 8-hexadecene-1,16-dicarboxylic acid is not employed in any of the various exemplary compositions of HARDING. In fact, none of the dioic acids, whether saturated or (mono- or di-) unsaturated, employed in the exemplary compositions of HARDING even contains 16 carbon atoms.

Regarding present claims 9 to 11 (which recite concentration ranges of 8-hexadecene-1,16-dicarboxylic acid in the claimed compositions) it is again pointed out that while HARDING discloses general concentration ranges of dioic acid(s) which (slightly) overlap the concentration ranges recited in claims 9 to 11, the concentration of the dioic acid(s) in the compositions of the various Examples of HARDING is at least 15 % by weight and is in most cases 20 % by weight, i.e.,

significantly higher than the upper values of the concentration ranges which are recited in present claims 9-11.

In this regard, it further is pointed out that one of ordinary skill in the art will understand that the broad concentration range for the dioic acids of 0.1 to 30 % given in HARDING for use in conjunction with retinol or a derivative thereof is due to the fact that the general formula of HARDING encompasses about two thousand different compounds (including stereoisomers) which can be expected to have very different activities. One of ordinary skill in the art will also understand that the fact that HARDING prefers a concentration range of 5 to 20% and employs dioic acids in the exemplary compositions thereof in a concentration of not less than 15% reflects the need for sufficient activity of the dioic acids in the compositions disclosed therein.

In this regard, claim 1 of HARDING makes it clear that an effective amount of from 0.1 to 30% by weight of a dioic acid must be employed. Accordingly, HARDING clearly does not teach or suggest that every dioic acid (or even only most of the dioic acids) encompassed by the general formula disclosed therein will be effective at a concentration of 0.1% but rather conveys the impression that an effective amount in most cases will be at least 15%, i.e., the minimum concentration of dioic acid(s) employed in the nine Examples of HARDING.

Moreover, a closer analysis of the Examples of HARDING shows that apparently the necessary concentration of dioic acid increases with the number of C atoms. Specifically, the only acids which are employed in a concentration of 15% (see Examples 3 and 9) are azelaic acid (nine carbon atoms) and a C<sub>8</sub> mono-unsaturated dioic acid. All of the other acids (having 12 to 22 carbon atoms) are employed in a (total) concentration of 20%. In view thereof, HARDING can even be considered to teach away from the subject matter of present claims 9-11.

Regarding the antioxidants which may be present in the compositions of HARDING, it is again pointed out that this document mentions antioxidants only in passing as one of many optional components of the compositions disclosed therein. Moreover, the only example of an antioxidant mentioned in HARDING, i.e., butylated hydroxytoluene, is a known antioxidant for foods (in contrast to, e.g., folic acid) and therefore, one of ordinary skill in the art would understand that antioxidants (and in particular, antioxidants which have nothing in common with butylated hydroxytoluene) do not play any special, let alone critical role for the intended effect of the compositions of HARDING but may optionally be employed, if at all, merely in order to protect various other components of the composition from oxidation. This understanding is supported by the fact that none of the compositions of the Examples of HARDING contains any antioxidant (not even butylated hydroxytoluene) and that HARDING does not even provide a concentration range for the optional antioxidants.

Regarding SCHONROCK, it is again pointed out that also this document mentions antioxidants only as optional components of the compositions disclosed therein and clearly fails to suggest that antioxidants play any particular, let alone critical role for the intended effect of the compositions disclosed therein. Applicants note that the Examiner relies on col. 12, lines 49-54 and appears to allege that this passage suggests (or even teaches) that antioxidants “play a role in lightening of skin”. Applicants respectfully disagree with the Examiner in this regard.

Specifically, SCHONROCK makes it absolutely clear that the only substances which are responsible for the skin lightening effect of the compositions described therein are the oligopeptides set forth in columns 1-5 thereof (see, e.g., title and col. 1, lines 60-64 and col. 10, lines 7-15). Antioxidants are mentioned in SCHONROCK only among a number of optional components which are “conventionally used” in cosmetic and dermatological preparations (see col. 12, lines 38-48).

Further, the passage in col. 12, lines 49-54 of SCHONROCK relied on by the Examiner states:

It is also advantageous to add customary antioxidants to the preparations in accordance with the present invention. Advantageous antioxidants which may be used in accordance with the invention are all those antioxidants which are suitable or conventional for cosmetic and/or dermatological applications.

It is not seen that the above passage suggests to one of ordinary skill in the art that antioxidants are critical or even only desirable components of the compositions of SCHONROCK, let alone critical components for achieving the desired effect of skin lightening. Further, SCHONROCK does not provide any indication at all as to why it is “advantageous” to add customary antioxidants to the preparations disclosed therein. Many other passages of SCHONROCK also use the terms “advantageous” and “advantageously” (see, e.g., columns 13 and 14) which makes it clear to one of ordinary skill in the art that these terms are not meant to highlight especially advantageous (optional) components of the compositions but merely are to indicate that the presence of these components is associated with the conventionally known advantages thereof (i.e., antioxidant properties).

It also is again pointed out that there is no motivation to combine HARDING and SCHONROCK because the compositions disclosed therein are entirely different with respect to their essential components. Moreover, the disclosure of SCHONROCK with respect to antioxidants does not add anything to the corresponding disclosure of HARDING, i.e., both documents mention antioxidants as optional components without mentioning any effect of these compounds which would go beyond their expected effect as antioxidants. None of the exemplary compositions of HARDING contains any antioxidant (indicating the lack of importance thereof), and it is not seen that SCHONROCK, i.e., a document which itself fails to suggest that antioxidants are important

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components of the compositions disclosed therein, provides any apparent reason for one of ordinary skill in the art to add any of the antioxidants mentioned therein to the compositions of HARDING.

Applicants submit that for at least all of the foregoing reasons and the additional reasons set forth in the response to the previous Office Action, the rejection of claims 1, 2 and 5-11 under 35 U.S.C. § 103(a) over HARDING in view of SCHONROCK is unwarranted and should be withdrawn, which action is respectfully requested.

***Response to Provisional Rejection of Claims***

It is again requested that the (assumed) provisional rejections of claims 1 and 2 on the ground of nonstatutory obviousness-type double patenting over claims of several co-pending applications be held in abeyance until the Examiner has indicated allowable subject matter.

**CONCLUSION**

In view of the foregoing, it is believed that all of the claims in this application are in condition for allowance (with the possible exception of obviousness-type double patenting issues), and a confirmation to this effect is again respectfully requested. If any issues yet remain which can be resolved by a telephone conference, the Examiner is respectfully invited to contact the undersigned at the telephone number below.

Respectfully submitted,  
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